REMARKS

The present Amendment and Request for Continued Examination is being submitted in response to the Office Action mailed January 15, 2010. Claims 71-76, 79 and 81-83 have been canceled without prejudice. New claim 85 has been added herein, and therefore after the entering of the present amendment, Claims 77-78, 80 and 84-85 will be pending in the present application.

On pages 3-4 of the Office Action the Examiner rejected claims 71-84 under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner rejected the claims because they contain both "comprising" and "consisting of language". Applicants have canceled claims 71-76, 79 and 81-83 without prejudice and have amended the remaining claims to only recite "consisting of" language. Based upon the present amendments, Applicants submit the rejection under 35 U.S.C. § 112, second paragraph has been overcome, and it is respectfully requested that the rejection be withdrawn.

On pages 4-7 of the Office Action the Examiner rejected claims 71-84 under 35 U.S.C. § 103(a) as being unpatentable over, Mehta *et al.*, United States Patent No. 5,837,284 ("Mehta") in view of Mulye, United States Patent No. 6,475,493 ("Mulye") and Beiman *et al.*, United States Patent No. 6,312,728 ("Beiman").

Claim 77 has been amended to incorporate the limitations of canceled claims 71, 74 and 79. Claim 77 recites a specific embodiment of the present invention, specifically claim 77 now requires the enteric coating to comprise a mixture of zein and at least one additional enteric polymer as taught by the examples of the present application. Additionally, claim 77 recites that the immediate release coating is applied to the enteric coating surrounding the compressed core. Further, claim 77 recites the specific *in vivo* and *in vitro* characteristics formerly recited in claim 71. Additional minor amendments have been made to correct claim dependency. New claim 85 has been added to further define an embodiment of the present invention, which recites 0.5-5 weight percent of a lubricant. No new matter has been added. Support for these amendments can be found in the claims as originally filed, and in the specification at page 4, line 21 to page 5, line 4 (*in vivo*

parameters); page 6, lines 6-24 (tablet formulation); page 7, lines 18-25 (lubricant); page 8, line 31 to page 9, line 8 (application of immediate release coating to enteric coating); page 9, lines 21-31 (*in vitro* release); and Examples 1-4 (tablet formulation and application of immediate release coating to enteric coating).

The Examiner stated on page 4 of the Office Action that because of the confusion with regard to "comprising" and "consisting of" language in the former claims, all claims were examined as if they were "comprising claims". Applicants submit that in view of the present clarifying amendments the amended claims are patentable over the prior art of record.

The present invention is an easy to manufacture controlled release methylphenidate tablet that contains a sustained release tablet core and an immediate release methylphenidate layer applied to the sustained release tablet core. The core of the present invention contains a compressed mixture of methylphenidate and a hydrogel polymer. The compressed mixture is then coated with a combination of zein and at least one additional enteric polymer. Unlike the prior art references, the release of the methylphenidate from the core is controlled and sustained in part by the hydrogel polymer. This sustained release is confirmed by the recited *in vitro* dissolution parameters recited in the claims. Specifically, the recited *in vitro* parameters require testing in a basic aqueous medium with a pH of 7.5, a pH where most enteric polymers readily dissolve. The sustained release of methylphenidate in a basic media is not disclosed or suggested by the prior art.

Mehta teaches a pulsatile dosage form comprising controlled release pellets wherein the coating on the pellets controls the release of the methylphenidate. Mehta does not teach or suggest a single compressed tablet core surrounded by a single enteric coating. The Examiner admits that Mehta does not disclose enteric coatings or the core materials recited in the pending claims. *See* Office Action at 5, first full paragraph. In addition to these deficiencies, Mehta fails to disclose the sustained *in vitro* parameters recited in the pending claims. Mehta's pulsatile delivery system is designed to provide an immediate release dose of methylphenidate within 15-30 minutes after ingestion, and a second burst or dose after a lag time. The second dose is delivered quickly, about 70-90% in about 0.5-2.5 hours, and preferably in about an hour. *See* Mehta, Col. 5, line 66 to Col. 6, line 17.

The tablet recited in the amended claims does not exhibit a rapid release of the second dose of methylphenidate. Rather, the tablet of the present invention requires a sustained release of the

second dose of methylphenidate. In fact, Mehta teaches away from the present invention on Col. 2, lines 42-49 wherein it states "sustained release formulations of methylphenidate have been shown to have lower efficacy than conventional dosage forms." This statement combined with the rapid release information of the second dose on Col. 5, line 66 to Col. 6, line 17 of Mehta would discourage a skilled artisan from preparing a hydrogel core that sustains the release of methylphenidate as recited in the present claims.

Mulye, like Mehta also teaches a multiparticulate or pelleted dosage system. Mulye requires the pellets to be coated with a coating comprising at least 75% of a water insoluble polymer and 1-25% of an enteric polymer. *See* Mulye at Col. 4, lines 30-38. Mulye provides no motivation to modify the teachings of Mehta and thereby arrive at the present invention. In fact, the teachings of Mulye are similar to the teachings of Mehta, because the coated cores exhibit a quick release of drug after a specific time period. For example, Col. 16, lines 45-60 of Mulye report the results of *in vitro* testing on dosage forms prepared according to Mulye. The data reports a slow release at low pH of about 1.2 - 4.5, but a "rapid release in pH 7.4".

Therefore, the addition of Mulye to Mehta would not lead a skilled artisan to the present invention which requires a tablet that slowly releases the methylphenidate at a pH of 7.5. At best the addition of Mulye to Mehta would lead a skilled artisan to believe the coating of Mehta can only be modified to include up to 25% of an enteric polymer. This amount of enteric polymer is substantially below the 45% required by the pending claims.

Moreover, Mulye directly instructs a skilled artisan not to use enteric materials that are insoluble in pH's greater than 4.5:

> The other ***necessary component of the coating is the enteric polymer which is essentially insoluble in an aqueous media at a pH at 4.5 or less***. In other words, it is substantially insoluble at 25°C in an aqueous media at pH's of 4.5 or less, e.g., the pH's typically found in the gastric juices, ***but is soluble in aqueous solution in pH's greater than about 4.5, for example, in pH's typically found in the intestinal fluid***. It is preferred that the solubility of the enteric polymer in aqueous media at pH of 4.5 or less at 25°C is 0.001 g/l. ***However, the enteric polymer is soluble at a pH above about 6.0 and especially in the range from about 6.0 to about 7.5***, i.e., the pH of the intestinal fluid, ***so as to permit release of the drug in the intestine and so as to not to substantially delay release therein***.

See Mulye at Col. 6, lines 8-21 (***emphasis added***).

Therefore Mulye does not disclose a dosage form that would provide a sustained *in vitro*

release of active in a basic (pH 7.5) environment, as required by the present claims.

The addition of Beiman to Mehta and Mulye will not overcome the above identified deficiencies and lead a skilled artisan to the present invention. Beiman, like Mehta and Mulye, teaches a pelletized dosage form and not an enteric coated compressed hydrogel tablet as recited in the pending claims. Beiman teaches coatings consisting essentially of enteric polymers that dissolve at a pH of 5.0 or higher. *See* Beiman at Col. 8, lines 61-65. Beiman further teaches that the pellets are designed to be coated with multiple layers that will provide doses of the drug at specific pH environments along a patient's gastrointestinal tract. *See* Beiman at Col. 6, lines 53-65. Beiman does not teach or disclose the possibility of a sustained release methylphenidate tablet containing a single enteric coating and a hydrogel core as required by the pending claims.

Applicants submit combining the disclosures in Mehta, Mulye and Beiman would lead a skilled artisan to a multi-particulate formulation with a coating that contains 1-25% enteric polymers, and which provides a pulsatile release of methylphenidate, in contrast to a compressed hydrogel tablet that releases the methylphenidate in a sustained manner at basic pHs.

Further, if the enteric coatings of Beiman were employed on either the Mulye or Mehta pellets, the resulting pellets would rapidly release the methylphenidate from the core when tested in an aqueous media with a pH of 7.5 as recited in the pending claims.

Because the cited prior art references do not disclose or suggest a methylphenidate tablet with a single controlled release coating containing a combination of zein and at least one additional enteric polymer surrounding a compressed hydrogel core, and wherein the tablet exhibits an *in vitro* sustained release of methylphenidate at a pH of 7.5, it is requested that the above 35 U.S.C. §103(a) rejection be withdrawn.

Based upon the above remarks, amendments and Request for Continued Examination, Applicants respectfully submit claims 77-78, 80 and 84 are allowable over the prior art and the present application is in proper form for allowance. Favorable consideration and early allowance is respectfully requested and earnestly solicited.

If the Examiner does not believe the pending claims are in the form for allowance, Applicants request the Examiner contact the undersigned to schedule an in person or telephonic interview to discuss ways to further expedite prosecution of this application.

Respectfully submitted,

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